

gives them the stimulus of teaching which is so essential.

A very popular clinic is that dealing with allergy. Here children suffering from hay fever and asthma are x-rayed, skin tested and treated. The large attendance suggests its necessity.

The Rheumatism and Cardiac Clinic should be under the supervision and care of a paediatrician with special training in cardiology. He should have first-class equipment if he is to do a good job. He must be supported by an efficient pathological laboratory and x-ray department and have the use of an electrocardiogram. He must be associated with an experienced cardiac surgeon. It should be possible to pick out from the mass of material offered, those cases suffering from rheumatism, cardiac disease and congenital malformations of the heart. His nurses should be able to visit the homes of the patients when necessary, and physiotherapy should be available both at the clinic and in the child's home, as well as modified education and occupational therapy. Long stay hospitals should also be available for such patients.

To illustrate the working of a health centre for children, I might mention briefly our centre started just one year ago in connection with the Vancouver General Hospital. A very old building, two stories high, and 40 feet square, was rehabilitated by a cheque from the Rotary Club. Generous citizens then gave the money to pay the staff for the first year. Figs. 1 and 2 show the record of our attendance as a whole, and of the attendance at each clinic, some of which as you will see, have just commenced.

The success of this venture depended on the quality of the service given and the co-operation of the Metropolitan Health Department of Vancouver. Only those patients were seen whose means conformed to the hospital standards for outpatients, namely, \$110 per month for man, wife and one child, rising by \$20 for each additional child.

Questioning the mothers of the children, it was apparent that 90% of this group of children who were largely referred by the school medical service, had seen no other doctor than the school doctor at any time and were able to make use of this service because it was free. It appears that this service did not in any way compete with the practices of the general prac-

titioner, nor the paediatrician, and the fact that the numbers have greatly increased suggests that the service was necessary in this community.

May I quote from that newest and monumental report of the American Academy of Paediatrics, 1949, on "Child Health Services and Paediatric Education".

"The modern hospital has become an essential of the social structure to which we are accustomed. It serves not only as a place where the sick may be given in-patient care but also a *health centre* for the entire community with its out-patient service, public health clinics, training for physicians and nurses and health education for the public. Without access to a good general hospital, no community is adequately equipped to fight against ill health."

To conclude, therefore, I would say that a health centre is not just a hospital outpatient department but it also embraces community services and public health services and these should be made available at all modern hospitals. An example of their need is shown by their attendance at the newly opened Health Centre for Children, Vancouver. It, I think, demonstrates the co-operation between curative and preventive medicine which is so essential if we are to offer complete health services to the community.

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## MODERN TREATMENT OF NEUROSYPHILIS\*

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THE observations and conclusions recorded in this paper are based on the experience obtained in the treatment of neurosyphilis, through the management of an out-patient venereal disease clinic and fever therapy department, associated with Victoria Hospital, London, for the past ten years.

The first thing in retrospect that strikes me, and I am sure it has been common experience, is the apparent ignorance or negligence of the physician, or lack of co-operation of the patient, which has allowed him to reach the advanced stage of neurosyphilis before a diagnosis is made. These cases have always appealed to me as a real tragedy, particularly when they reach

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\* Read at the Annual Meeting of the Ontario Neuro-psychiatric Association in Toronto, February 18, 1949.

the advanced stages of paresis, tabes dorsalis, or when total blindness intervenes. This of course refers to the management of such cases in general practice, and indeed I may say in the medical practice of specialists. I believe that the mental health clinics, co-operating so admirably in various centres, have a special function in picking up these neglected cases. Constant vigilance must be exercised if one is not to be caught napping. It should be routine procedure to do a spinal fluid examination; not only in the adults but on the child of teen-age with vague neurological symptoms, who may surprise you with a positive spinal fluid.

Although there is a relatively higher overall percentage increase of neurosyphilis, compared to early syphilis,\* reported from 1944-48, there is a decrease in the total number reported to the Venereal Disease Division of the Ontario Government (1944-48). This would indicate that the improved epidemiological set-up in the province is getting these patients under adequate treatment earlier. I think it is well borne out in our local situation, in the London district, where the admission rate to the Ontario Hospital has been reduced yearly. On further scrutiny, however, it was found that this reduction locally was greater than the reduction in the admissions of neurosyphilitic patients in all the Ontario mental hospitals (see Table I). This is un-

the advanced stages requiring Ontario hospital attention. It is indeed an enviable situation maintained by the Ontario Division of Venereal Disease Control, wherein the cost of hospitalization and the fever cabinet personnel have been made so freely available to the public. This has been broadened to include the free administration of penicillin to such patients, as well as other forms of chemotherapy.

Recent authoritative studies with the use of penicillin in the treatment of neurosyphilis indicate, without a doubt, that it is the drug of choice. Its relative lack of toxicity, shorter duration of therapy and the phenomenal response, especially of the spinal fluid serology, give it preference over the various older drugs formerly utilized, such as arsphenamine, mapharsen, neoarsphenamine and the pentavalent group, tryparsamide, acetarsone or aldarson, combined with the heavy metals and iodides. Its relative merits in relation to fever therapy is a controversial question at the moment. It should be borne in mind, however, that the care of the neurosyphilitic patient, as in other forms of syphilis, should be individualized. The type of treatment for a particular patient should be determined by the age, physical status, duration and variety of involvement of the nervous system. Neurosyphilis may not respond to one form of therapy and yet may show remarkable improvement with another.

The above facts would not seem to warrant such statements as made by Dattner<sup>1</sup> and his associates as follows: "We believe that penicillin will ultimately replace fever therapy", or by Curtis<sup>2</sup>, who states: "Even in tabo paresis and paresis, there are indications that penicillin alone will eventually prove as effective as in combination with malaria". On the other hand, O'Leary<sup>3</sup> states: "Although it is too early to compare the value of penicillin with that of other methods used in the treatment of neurosyphilis, my experience indicates that penicillin produces clinical improvement in from 15 to 20% of cases, while fever therapy produces improvement in from 60 to 80% of cases". Experimentally, Eagle, Magnuson and Fleischner<sup>4</sup> find a striking increase in the efficacy of penicillin vs. rabbit syphilis, when the drug was given in conjunction with fever therapy. Reynolds, Mohr and Moore<sup>5</sup> present a comparative study and conclude: "The effectiveness of concurrent penicillin-malaria therapy is such as to make it, for the present at least, the treatment

TABLE I.  
PERCENTAGE OF NEW ADMISSIONS OF NEUROSYPHILITIC PATIENTS

	To all Ontario hospitals	To Ontario hospital, London
1937 .....	5.3	5.5
1938 .....	6.3	4.1
1939 .....	5.5	3.7
1940 .....	5.6	2.5
1941 .....	6.1	3.3
1942 .....	5.0	3.0
1943 .....	4.5	3.1
1944 .....	5.3	2.6
1945 .....	5.3	2.7
1946 .....	4.4	2.1
1947 .....	3.7	2.6

Showing the greater decline in the admission rate of neurosyphilitics in the Ontario Hospital, London, as compared to all the mental hospitals of the province.

doubtedly due, in part, to the establishment in 1938 of a fever cabinet centre in Victoria Hospital, London, which resulted in concentrating potential Ontario hospital patients to the Clinic, where many have been prevented from reaching

\* Early syphilis is being reduced by the intensive treatment schedules introduced.

of choice for patients with dementia paralytica". An article by Stokes<sup>6</sup> states: "In tabo paresis and meningovascular neurosyphilis, the results with penicillin are serologically superior and clinically equal to those with malaria". Interestingly he postulates that in the treatment of paresis, malaria fever usually shows more clinical improvement in the first year than penicillin; but that penicillin overtakes in the second and surpasses malarial therapy in the third year after treatment. Similar results are found in tabo paresis, meningovascular lues and tabes.

These divergent opinions, are, to my mind, well summed up by Solomon<sup>7</sup> who states:

"This is very reminiscent of the difference of opinion which has occurred over the years as to the relative effectiveness of trypanamide, malaria and mechanically produced fevers. After exhaustive studies over a period of more than twenty years, no uniformity of opinion was reached. It is therefore not surprising that opinions should differ with regard to penicillin and it is probable that general agreement will not be attained in the course of a number of years."

Already, in my experience, cases where fever therapy was successful following an apparent penicillin failure, have been encountered. Three examples are listed below. One might go further and suggest that arsenicals of the pentavalent group such as trypanamide, still have a place with iodides and heavy metals in the management of the patient resistant to the more accepted forms of therapy. This brings into play not only a specific attack vs. spirochaetes and its variants; but a consideration of the resistance of the host. This latter would argue in favour of the addition of fever therapy in its safest modality, in view of its apparent stimulation of the defensive mechanism of the patient.

#### CASE 1

R.C., aged 37, with transverse myelitis, reported to a doctor, August 14, 1944, suffering with a penile chancre and bilateral inguinal adenopathy. A blood Wassermann proved positive with a quantitative titre of Kahn 4 units. He was given 8 injections of mapharsen 0.04, and 11 injections of bismuth salicylate gr. ii (intramuscularly). The arsenical injections were temporarily stopped because of upper respiratory infection. On November 30, 1944, the patient complained of severe pain in his left leg, paraesthesia and ataxia. He was transferred to hospital where total paralysis occurred with complete loss of bladder and rectal function. Penicillin therapy was administered both intramuscularly and intrathecally in 3,000,000 units dosage, with little or no improvement. On further medical advice he was referred to fever therapy. At this time a neurological examination revealed "almost complete paraplegia below D 10 with a complete loss of posterior column sensitivity and almost complete paralysis (there being slight improvement in the right leg) with diminished to absent reflexes and a positive Babinski, retention of urine, complete loss of pain and temperature over lower abdomen.

Patient was admitted to Victoria Hospital, London, Ont., January 19, 1945. A cerebrospinal fluid examination was made January 22, resulting as follows: cell

count, 21 per c.mm.; Wassermann, 41,000; total protein 129 mgm. per 100 c.c. Colloidal gold reaction 555421000. On February 9, fever therapy was initiated. This was continued at weekly intervals to a total dosage of 68½ hrs., at 105.4° F., along with 10 injections of aldarson, given in gm. dosage at weekly intervals. Improvement became very rapid, and, at completion of fever therapy, bladder and rectal sphincter control had improved and he was able to walk with the use of a cane or crutches. He was discharged from hospital March 28, and was able to return to his former occupation as a truck-driver. Another spinal was made June 25, with the following results; Wassermann 44,100, total protein 40 mgm. per 100 c.c., colloidal gold reaction unchanged.

*Comment.*—This case was formerly reported by me with the prediction that in the future, fever plus penicillin therapy might be the method of choice in the management of parenchymatous neurosyphilis.

#### CASE 2

R.K., aged 61, with paresis. This case came under my care in the latter part of April, 1948, with signs of early paresis as designated by a slight depression. His spinal report as of November 8, is as follows; cell count, 0 per c.mm. Wassermann 44400 (very strongly positive). Total protein 50 mgm. per 100 c.c., colloidal gold reaction 222210000.

He was hospitalized, receiving 6,000,000 units of penicillin over a period of 2 weeks, and discharged under observation. About the first of November, I received a telephone call from his physician that this man was acting in a peculiar manner, exercising poor judgment in his business dealings and spending his funds indiscriminately on various projects. For instance, he was at the moment in Toronto, negotiating the purchase of a \$1,300.00 yacht for his minister. He had written cheques for various large sums to public organizations. He was persuaded to return to me for further treatment and on November 8, was admitted to Victoria Hospital. The patient had delusions of possessing great wealth and was obviously suffering from grandiose ideas and was very euphoric. This man was undoubtedly a candidate for the Ontario Hospital, in spite of his initial penicillin therapy. However, it was decided, despite the hazards accompanying his age, 61 years, that we give him fever therapy. In January, 1949, he completed 70 hours of fever therapy at a temperature of 105° F. A cerebrospinal fluid examination was made on February 16, which revealed a cell count of 2 per c.mm., Wassermann 44400, total protein 50 mgm. per 100 c.c., colloidal gold reactions 34421000. Apparently he made a complete remission of his symptoms and appeared his normal, non-aggressive personality. He was modest and retiring and very much his old self.

Having a complete insight into his former state, he felt keenly the shame and embarrassment afforded his family. On discharge from hospital, February 10, it was felt that a probation period of at least a year should elapse before the responsibility of his business should be returned to him. This was unfortunate, as circumstances necessitated his returning to his former environment, where he lived by himself and put in his time around his place of business where he felt frustrated. He was interviewed at weekly intervals with no apparent personality change; but some evidence indicating the above situation was elicited. On April 11, he apparently felt his situation impossible and committed suicide.

*Comment.*—I feel that if this patient had been given fever and penicillin therapy when first observed that the above tragedy might not have occurred.

#### CASE 3

L.C., aged 55. This man was diagnosed as a tabetic; but presented a negative cerebrospinal fluid and a negative blood Wassermann. There was some evidence of

paretic involvement. His chief complaints were intractable lightning pains. 5,000,000 units of penicillin therapy did not afford any relief and a month later it was thought advisable to administer fever therapy, which was completed November 8, 1948, to a total of 69 hrs. at 105° F. Since the instigation of fever therapy, he has improved mentally, and although he has an occasional twinge, the so-called "lightning" pains are practically under control. In addition there is an improvement in his gait.

In view of these experiences, for in-patients at the London Clinic, we give penicillin alone, intramuscularly, in dosages varying from 6,000,000 to 10,000,000 units in individual doses of 50,000 units at 3 hour intervals, over a period of from 2 to 3 weeks, in asymptomatic neurosyphilis, meningovascular, cerebrovascular and gummatous involvement of the central nervous system. In out-patient ambulatory patients, we have arbitrarily been using 3 intramuscular injections weekly of 600,000 units dosage of procaine penicillin, to a total of 12,000,000 units. If there is no clinical improvement and serological investigation does not reveal that the process has been definitely checked, fever therapy is instituted, and, in addition, chemotherapy, consisting of further penicillin and tryparsamide or aldarson with heavy metals may be included.

In dealing with paresis, tabes dorsalis or tabo paresis, Erb's spastic paralysis or optic atrophy, *penicillin plus fever therapy* is combined from the first. We do not feel that fever therapy should be administered in reduced amounts as suggested by Solomon.<sup>7</sup> In these cases, six to 10 million units of penicillin, combined with 70 hours of artificial fever therapy at 105° F., is the routine practice. In most cases where the disease is not too advanced, the patients are treated on an ambulatory basis, returning at weekly intervals for successive treatments (usually from 10 to 12). During the initial investigation period penicillin is commenced and is continued during the active treatment period, in the cabinet, and subsequently to the total dosage designated. The patient then returns to his home for employment in the midweek interval, until the course is completed. The use of electroshock treatments to initially acquire the co-operation of an agitated patient would seem to be of value. This procedure has been used on occasion.

During the past ten years, 200 patients, made up of all varieties of neurosyphilitics, have received artificial fever therapy; 40% were of the paretic type, comprising a total of 11,500 hours, averaging 56½ hours a patient. In this group,

3 deaths have occurred, directly or indirectly attributable to fever therapy. Considering the range of ages from 8 to 65 years, and the seriousness of the disease treated, combined with the natural vascular degenerative processes which occurs in the older age group, the associated risk does not seem to be prohibitive. Repeated efforts are being made to procure follow-ups on the patients treated, who, for the most part, are referred from many distant points. When possible, spinal fluid examinations are obtained every six months for two years following therapy, and then at yearly intervals, until the disease is considered definitely under control.

Lumbar tap is the routine method for obtaining spinal fluid. Cisternal puncture however is utilized where the patient becomes apprehensive, by repeated post-puncture headaches or backaches. This is a useful procedure in an out-patient clinic, where some patients refuse to co-operate, owing to hearsay. Headaches and backaches do not occur.

Prior to fever therapy, a complete physical and laboratory examination is carried out, including x-ray and electrocardiogram. The services of the consulting medical staff of Victoria Hospital, including a psychiatric opinion are freely utilized for the purpose of acquiring the best clinical evaluation of his ability to withstand the rigours of therapy and the truest picture of the neurological involvement. The cases are selected for fever on the basis of their ability to withstand the ordeal, and in borderline cases, one does not hesitate to weigh the associated danger against the dismal outcome of a rapidly progressing case. This decision is not unlike that of a surgeon who accepts the hazards of an operation to save an otherwise hopeless case.

No effort will be made here to evaluate the findings on a statistical basis. The results of therapy are reflected to not a little degree in the continued decline in the number of admissions of neurosyphilitic patients to the Ontario Hospital in the London district.

*Treatment reactions.*—A recapitulation in this paper of the reactions encountered in the use of heavy metals and arsenicals does not seem to be advisable, as this should be common knowledge. The reactions and complications occurring in the course of the actual fevering of the patients is the particular responsibility of the attending personnel.

The present establishment of penicillin as the drug par excellence, in the treatment of neurosyphilis, focuses attention at the moment on the possible reactions encountered in its usage. Certainly penicillin alone is the least hazardous of all these drugs. The reactions have been classified<sup>8</sup> briefly: (1) Primary irritant. (2) Therapeutic shock. (3) Allergic manifestations.

The Jarisch-Herxheimer reaction may be focal or systemic and symptoms will usually subside in 24 to 48 hours. In central nervous system involvement, these symptoms may be avoided by low initial doses of the drug. This is particularly applicable when complicated by cardiovascular involvement. The following reactions<sup>11</sup> are reported, exacerbation of psychosis, convulsions, transverse myelitis, mania, hallucinations, lightning pains, rapid paretic deterioration, progressing to death and progression of tabetic primary atrophy to blindness.

At the present time, apart from therapeutic shock, the greatest number of penicillin reactions<sup>8</sup> will fall under the "allergic" classifications. Sensitivity may appear immediately or after a latent period. Sensitivity may be acquired through exposure to penicillin; but a few may be spontaneously susceptible. The acquired form is analogous to drug or serum sickness and reactions are sometimes characterized by resemblance to delayed serum sickness. If a bullous eruption or eczematous id appear, extreme caution should be exercised in further treatment.

Lamb<sup>9</sup> has recommended that each patient be questioned as to a history of allergy and previous penicillin sensitivity and trichophytosis, or other infections. Allergic reactions respond frequently to the withdrawal of the drug, to cold applications and to the use of anti-histamine drug.

#### SUMMARY AND CONCLUSIONS

Penicillin is the modern drug of choice in the treatment of neurosyphilis, because of its low toxicity and high therapeutic effect. The results of therapy are apparently equal to and often may exceed other methods of chemotherapy. It is undoubtedly the least hazardous of the drugs. A course of 10,000,000 to 12,000,000 units alone, administered over a period of two to three weeks, is in most cases sufficient in the

management of asymptomatic neurosyphilis, acute syphilitic meningitis, meningovascular and cerebrovascular lues or gumma. The gauge of progress in treatment should be the serological reversal of active manifestations as indicated by the cell count, total protein, colloidal gold and complement fixation tests. Failure to respond, however, as indicated by the onset of symptoms, or lack of serological improvement within six months to one year, should necessitate a repetition of penicillin preferably combined with fever therapy.

The present day enthusiasm for the use of penicillin alone as the ideal therapy based on the spectacular response of the spinal fluid serology is not entirely warranted. In spite of serological arrest of activity, the patient who does not show symptomatic improvement should have the additional effect of fever therapy, combined with penicillin and possibly the addition of an arsenical. We must not lose sight, as clinicians, of our responsibility to the individual in such cases.

Attention is directed to the possibility of reactions encountered in the use of penicillin in neurosyphilis.

Several years of observation will be required to see the ultimate effects of penicillin alone in asymptomatic neurosyphilis. Confused reports as to its efficacy, in comparison with fever therapy alone, or combined with fever therapy, in the treatment of symptomatic neurosyphilis are permeating the literature.

It would seem that until the results of penicillin therapy alone are evaluated in the course of time, that penicillin, plus fever therapy, and, in selected cases, arsenicals and heavy metals, should still be the choice of treatment of advanced or resistant neurosyphilis.

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